REVIEW ARTICLE

Environmental Costs of Pain Management: Pharmaceuticals Vs Physical Therapies

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Abstract

Analgesics are among the most widely used medications in America, and their use is growing rapidly. As a result, the environment is becoming increasingly contaminated with analgesic residues created by the manufacture, consumption, and disposal of these medications. Most analgesic residues that end up in wastewater are not destroyed during treatment in wastewater treatment plants (WWTPs), and so they are accumulating in surface water, ground water, drinking water, and sludge; municipal landfills are also accumulating loads of unused medications.

For most Americans, these residues constitute a long-term, low-level exposure to analgesics and mixtures of different analgesics—as well as to whatever other pharmaceuticals residues are in their environment. As health-care professionals become more aware of the growing concerns of the scientific community and federal regulatory agencies, effective nonpharmaceutical approaches to pain management may become more attractive.

Manufacture of pharmaceuticals creates toxic waste, requires more infrastructure, and consumes far more energy and raw materials than the use of physical therapies does. Future environmental cleanup costs are also part of the total true cost of managing pain with analgesics. This article provides an overview of the ways in which analgesics are entering the environment, current scientific concerns regarding adverse effects on wildlife and humans, and research on the effectiveness of physical therapies to treat pain. In terms of toxicity to the environment, pain management with physical therapies is superior to management with analgesics.

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Analgesics are among the most widely used medications in America and their use is growing. Analgesics are used to relieve pain, including (1) chronic pain from conditions such as neck and back dysfunction, headaches, and pelvic pain; dysmenorrhea, arthritis, cancer, and fibromyalgia and (2) acute pain from such conditions as physical trauma, postoperative swelling, and internal-organ problems (eg, renal colic). Many sufferers take analgesics that their physicians have prescribed, such as nonsteroidal anti-inflammatories or NSAIDs (ibuprofen, aspirin, and naproxen), opioid analgesics, (codeine), or combinations of the two (hydrocodone, oxycodone). People also use nonprescription analgesics (aspirin, Tylenol) and analgesic gels widely.

In 2010, physicians wrote 131 million prescriptions for hydrocodone (Vicodin), making it the number-one prescribed medication in the United States; oxycodone and ibuprofen were in 21st and 22nd place, respectively.[1] Many other analgesics are among the most frequently prescribed of all medications. In 2010, physicians prescribed enough narcotic painkillers to medicate every American adult around-the-clock for a month.[2] One indicator of the increasing popularity of these medications is the number of deaths from overdoses of prescribed narcotics: this number nearly quadrupled between 1999 and 2008, and currently amounts to 40 Americans each day.[3,4] The increasing use of opioids by pregnant women has resulted in a great increase in the number of infants born opioid-addicted.[5]

Another unappreciated side effect of widespread use of analgesics is the increasing contamination of the environment with its residues. Pharmaceutical manufacturers design modern medications to be long-lasting and to retain their chemical structure long enough to do their therapeutic work: this means only 25% of all medications rapidly degrade into innocuous products when they enter the environment.[6] Some analgesics have a long half-life and thus tend to accumulate. For example, naproxen (Aleve) remains intact for at least 1 year.[7]

Even if analgesics' active pharmaceutical ingredients (APIs) degrade to some extent, their widespread use continually introduces more residues and so significant concentrations remain constant in the environment. Consequently, analgesics are now ubiquitous in surface waters. When Philips et al tested 139 streams in 30 American states for measurable amounts of pharmaceuticals, 80% of the waterways showed traces of common medications, including analgesics: 24% contained acet-

aminophen, 11% contained codeine, and 10% contained ibuprofen.[8] Analgesic residues can now be found in groundwater, surface waters, treated drinking water that is taken from surface waters, and in sewage-treatment plant sludge, which is often spread on farmland.

How Contamination Occurs

Analgesics are entering the environment in three distinct ways: (1) via manufacturing, (2) through consumers' use, and (3) through disposal of unused medication.

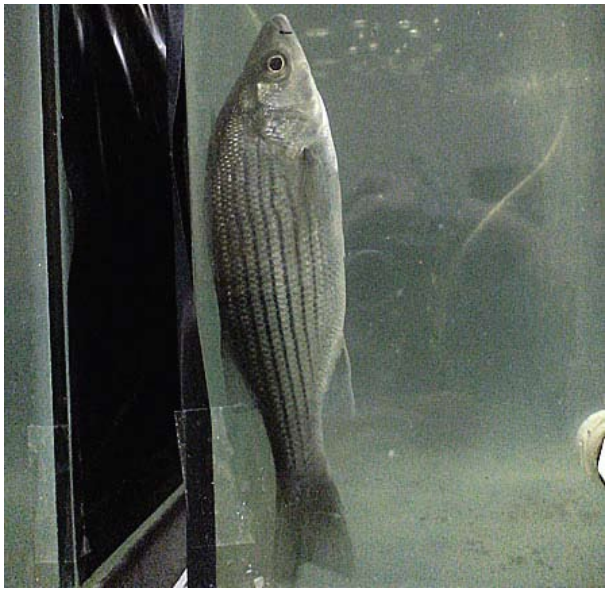
Manufacture. Current manufacturing processes often lead to discharges from factories of water containing APIs directly into waterways. The manufacturing process requires large amounts of water, and the resulting wastewater contains considerable pharmaceutical residue. Scientists have found opioids, including oxycodone and methadone, in the effluents of wastewater treatment plants (WWTPs) that receive water from pharmaceutical factories. These effluents have concentrations 10 to 100 times higher than typically found in other WWTPs effluents.[9] APIs can also contaminate well water near manufacturing facilities.[10]

Consumption. Consumers inadvertently contaminate water through their use of analgesics. Humans excrete a proportion of most medications, and their urine and feces, which contain unabsorbed drugs or drug metabolites, go down the toilet directly into the domestic sewage system. Bathing also transfers the residues of analgesic gels, creams, and pain patches from the skin into the drain. Humans can excrete opioids in sweat, and bathing sends those chemicals directly into the sewer system as well.[11-12] These data are true not only for individuals in their own homes but also for patients at long-term care facilities and hospitals. Hospital wastewater, often left untreated before it enters the domestic sewage stream, often contains significant quantities of analgesics and other medications.[13-17]

Disposal of Unused Medication

Disposal often contributes to contamination. Flushing unused or expired analgesic pills or patches down the toilet sends them directly into the domestic sewage system. Disposing of them in the home garbage sends them directly to landfills, and there, with few exceptions, they are leached out by rainfall and dissolved back into ground and water systems. Long-term care facilities, hospices, hospitals, and individuals all contribute to this problem. Because of adverse effects, resolution of health problems, or switches to other medications, patients actually never take a surprising amount of their prescribed medications. Every year, upwards of $1 billion of prescribed medications go unused by American seniors who generally flush these medications down the toilet or place them in their home garbage.[18-19] Some local and state-based disposal processes now take back a small proportion of these unused medications.

Figure 1. Exposure to dilute quantities of human pharmaceuticals can affect aquatic animals. For example, when exposed to the antidepressant Prozac, this hybrid, striped bass eventually stopped eating and began hanging vertically rather than swimming.



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In Washington State, with a population of 6.25 million, every year consumers do not use an estimated 33 million containers of pills—amounting to 82,000 pounds of medication.[20] Nursing homes generate 8% of this total.[21] Hospitals and long-term facilities throw away 250 million pounds of pharmaceuticals and contaminated packaging each year, including partially used vials, outdated medications, intravenous equipment and syringes as well as the equipment, solutions, and materials used in general compounding and preparation of medications.[22] Much of the unused medication is analgesics. In one take-back event in Maine during which consumers could return unused medications, analgesics were 13% of the total returned medicines, making them the single most common type of unused or expired medicine.[23] In another take-back event in California, the most common type of returned medication was analgesics, such as ibuprofen, acetaminophen, and aspirin.[24]

Why Contaminants Remain in Treated Wastewater

Ideally, wastewater treatment removes analgesic residues. WWTPs, however, are not specifically engineered to remove pharmaceuticals, and removal efficiencies vary widely. Most analgesic residue remains after treatment. As far back as 1977, researchers found analgesic residues were present in sewage effluent, the treated water that flows out of the WWTP.[25] In 1998, a German researcher tested efflu-

ent from a WWTP and detected 24 different medications, including many analgesics.[7]

Conventional water-treatment processes are still unable to remove pharmaceutical compounds efficiently.[26] Reverse osmosis and activated charcoal treatments will work for many compounds, but they are not widely used in WWTPs due to their expense.[27] Treatment through reverse osmosis generates a contaminated effluent that varies from 20% to 35% of the total treated water. The plant must then dispose of that effluent or evaporate it down to solids; its contaminants do not simply go away.

Accumulation in Water, Soil, and Landfills

Although the effluent of WWTPs is greatly diluted once it flows back into waterways, scientists can still identify analgesic residues in surface waters all over the world. Of the 18 most commonly detected medications in effluents from American WWTPs, five are painkillers.[28] The effluent that flows from the WWTP in Las Vegas, Nevada, into Lake Mead has contaminated that body of water with detectable levels of hydrocodone and codeine.[29] Effluent entering streams from WWTPs in one region of Pennsylvania has caused consistently high levels of acetaminophen.[30] In one region of western Washington State, scientists detected acetaminophen, codeine, hydrocodone, and ketoprofen in the effluent of WWTPs.[26]

These rivers, streams, lakes, and reservoirs are the sources of the water that is the genesis of drinking water. When scientists collected samples of both untreated and finished drinking water (water ready to drink) from 20 drinking-water plants across the United States, they detected ibuprofen in over 65% of the samples; treatment had removed only small amounts of it.[28] It is important to note that the analytical methods currently available to scientists may not be capable of detecting many of the pharmaceuticals that they have identified as potential problems. Nor can the consumer necessarily avoid drinking analgesic-tainted water by switching to bottled water; that water commonly contains residues of pain medications, such as acetaminophen.[31]

Analgesic residues are also accumulating in locations other than bodies of water. For example, when humans use wastewater containing APIs (analgesics, antidepressants, antibiotics, estrogens) for irrigation, those chemicals can persist and even accumulate in soil.[36] In one study, tested sludge contained high levels of acetaminophen and ibuprofen.[37] When individuals spread sludge containing APIs on farmland, growing plants absorb at least some APIs.[38]

Scientists have found APIs, including analgesics, in high concentrations in municipal landfills, where they can mix with rainwater and eventually exit the landfill in leachate. Humans even sometimes place sludge containing APIs in landfills. Numerous wells that are downgradient from landfills containing thrown-away medications have tested positive for acetaminophen and ibuprofen in their water.[39-41]

Implications of Contamination

Effects on Aquatic Animals and Humans

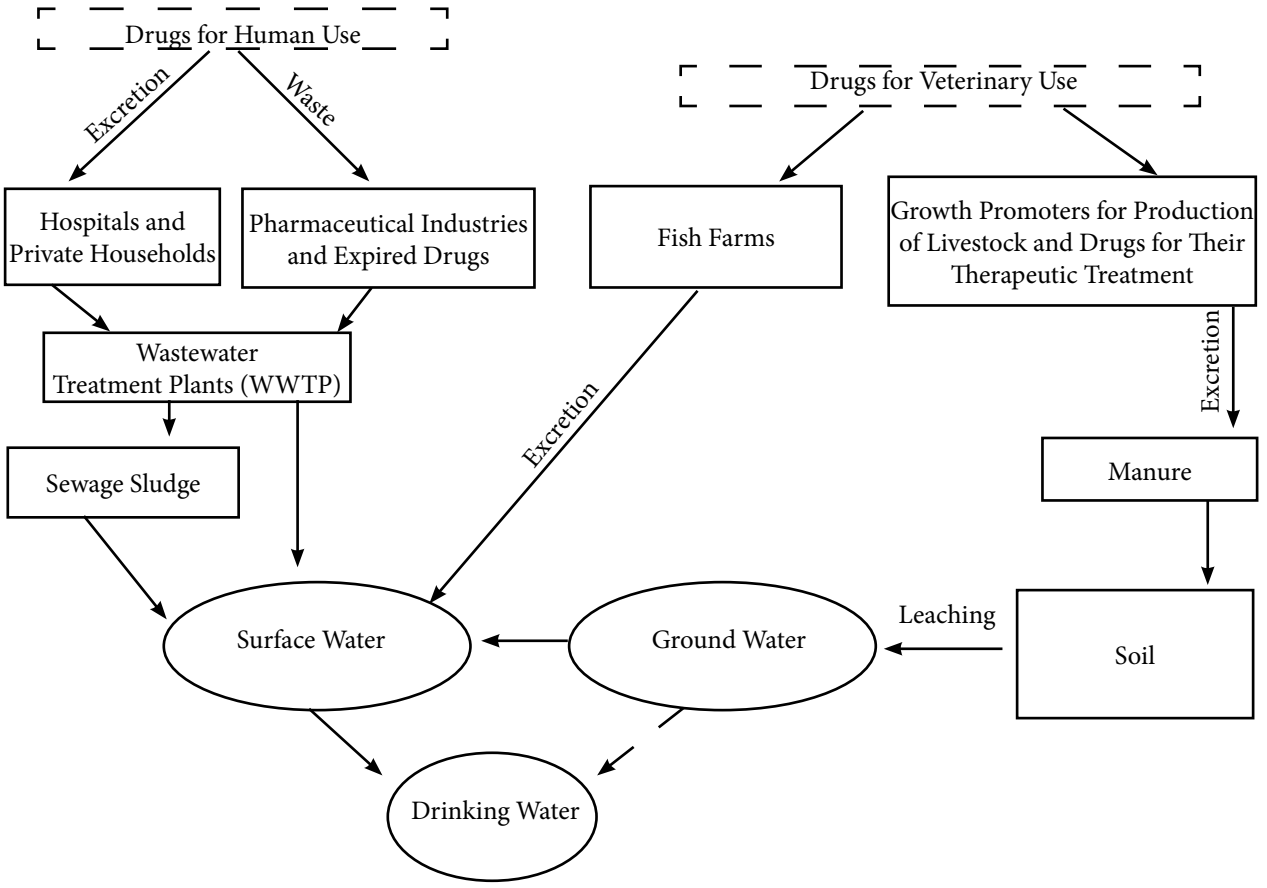
As the situation stands today, water treatment is not significantly reducing analgesic residues, and widespread consumption keeps residues at high levels. What are the hazards of this situation? Scientists are concerned about a number of issues.

Effects on Aquatic Animals. Long-standing exposure to even small concentrations of APIs can have subtle adverse effects upon aquatic animals. Researchers have linked exposure to physical abnormalities, higher death rates in the young, impaired ability to reproduce, feminization of male fish, decreasing populations, and changes in many different behaviors.[42-45] For example, fish that were exposed to the antidepressant Effexor as hatchlings

Table 1. The table shows analgesics detected in water sources of selected American cities, in either (a) untreated water before the city's drinking-water plant treats it or (b) finished water after the drinking-water plant treats it.

Location	Analgesic Found	Type of Water Source
Las Vegas	Hydrocodone+codeine	Water from Lake Mead, untreated[29]
New York City	Ibuprofen	Water from the Hudson River, untreated[8]
Erie, Pennsylvania	Ibuprofen	Water from Lake Erie, treated by city[32]
Philadelphia	Acetaminophen Aspirin Diclofenac Ibuprofen Naproxen	Water from Schuylkill and Delaware Rivers, treated by city[33]
New Orleans	Naproxen	Water from the Mississippi River, treated by city[34]
Ann Arbor, Michigan	Acetaminophen Ibuprofen	Water from Huron River, untreated[35]

Figure 2. How Pharmaceuticals and Their Metabolites Enter the Water Supply



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reacted much more slowly than normal to predators, which could result in increased mortality.[46] Effects on wildlife may occur even at concentrations below one part per billion.

Effects on Human Health. The reality of Americans' cumulative exposure to low concentrations of random and complex mixtures of pharmaceuticals has caused widespread concerns about the potential effects on human health, including increased risk of cancer, increased antibiotic resistance, genetic alterations or mutations, and reduced fertility due to endocrine disruption.[7,47] Of particular concern is the exposure of sensitive subpopulations during certain critical periods, such as fetuses, infants, children, women of child-bearing years, invalids, the elderly, and people with suppressed immune systems. Even if a pharmaceutical company has proven a medication's safety for its target population (ie, cholesterol-lowering medication for adults with high cholesterol levels), it has not evaluated the potential for adverse effects in nontarget populations.

Because the widespread use of pharmaceuticals is a recent development, research to determine safety has lagged behind their introduction into the environment, and so the effects on human health of exposure to analgesics and other pharmaceuticals are poorly understood.[47] At this point, no definitive evidence exists that high concentrations of APIs, including analgesics, can have adverse effects upon humans, but scientists point out that absence of evidence is not proof of safety. More research is needed.

Humans have introduced many substances into the environment that they once thought to be benign but later found to be hazardous. For example, scientists now know that benzene, once widely used and considered safe for most of the 20th century, is actually highly toxic, and the Clean Water Act strictly regulates it. Scientists also thought dioxin was benign but later discovered it to be highly carcinogenic and damaging to the immune and reproductive systems. The US government now highly regulates releases of dioxin.

When tested, concentrations of APIs, including analgesics, in surface waters are usually low, in parts per billion or trillion.[27] However, humans consume water in sizeable amounts each day, which creates a lifelong, low-level exposure to chemicals and combinations of chemicals that have been specifically formulated to have potent physiological

effects upon the body. Nor is the average person likely to be exposed to one pain medication only; scientists frequently find residues of multiple analgesics dissolved in water.

Ultimately, analgesic residues may become part of a complex mixture of bioactive compounds, including residues from antibiotic, estrogen, antidepressant, cholesterol–lowering, and anticancer medications. Street drugs, detergents, pesticides, and other unknown chemicals may also be present as part of the mixture.[45,46] The concentrations of some drugs in water are comparable to the low-parts-per-billion (ppb) levels at which scientists typically find pesticides.[48,49] Pain medications are a significant part of this mix; on a 2008 list of the 16 pharmaceuticals that scientists consider the most worrisome given the amount sold and excreted into the environment each year, three were analgesics.[46] Of the 20 compounds from prescribed medications that are most likely to be found persisting in waters, five are analgesics—acetaminophen, diclofenac (Arthrotec, Voltaren, and Cataflam), hydrocodone, ibuprofen, and naproxen.[27]

Ecological Effects of Manufacturing

One final aspect of the effect of pain medication upon the environment is the ecological effects of the manufacturing process. Production facilities require an extensive infrastructure, and, once online, consume large amounts of raw materials, water, and energy. The pharmaceutical industry in the United States consumes about $1 billion in energy each year.[50] It also uses 100 kilograms of solvents, reagents, water, and other ingredients to produce 1 kilogram of medication.[6]

Pollution is part of the picture as well; each year, pharmaceutical manufacturing facilities create and release millions of pounds of air, water, and soil pollutants, including carbon monoxide, nitrogen oxide, particulate matter, sulfur dioxide, and volatile organic compounds. Manufacturing also produces waste, much of which is toxic; 80% is spent solvents such as benzene, toluene, heptane, and chlorobenzene. Water used in cleaning equipment contains significant residue and is toxic as well.

Manufacturers are working toward developing more sustainable systems, but so far they have emphasized efficiency rather than environmental effects. Environmental cleanup costs should be figured in when we try to determine the total true environmental cost of the use of analgesics.[51,52] By contrast, clinics and spas that offer physical therapies, including exercise, massage, and hydrotherapy treatments, do not use huge amounts of water and energy, and they create only minimal contamination of water. Their construction is far less resource-intensive than pharmaceutical factories, and their operation produces only a tiny fraction of toxic waste with its attendant cleanup costs.

Difficulty of Finding a Solution

Ultimately, it simply may be beyond the capabilities of science to sort out the many chemical interactions that can occur in complex chemical mixtures of water and medications. This reality gives rise to a number of questions. Does the possibility exist that analgesic residues could bioaccumulate in fish that humans eat? Schwaiger et al have shown that one NSAID, diclofenac, accumulates and causes pathologic changes in the kidneys and gills of rainbow trout.[53] If humans eat such chemically affected trout, could that food be toxic? One of the most common raptors in Pakistan, the Oriental white-backed vulture, became virtually extinct after veterinarians there began feeding veterinary diclofenac to cattle. Vultures that fed on carcasses soon died of acute kidney failure.[54]

Diclofenac is currently the single most ubiquitous pharmaceutical in the environment.[55] What happens to humans who eat fish with this medication stored in their tissues? Pomati et al found that a mix of 13 common medications frequently found in drinking water inhibits cell growth in human embryonic cells.[56] What exactly does this finding mean for human health? Without further research, it is impossible to say.

As they learn more about pharmaceutical contamination of our environment, professionals in the health-care community have begun to consider ways that they can help decrease the environmental footprint of pharmaceuticals.[57-60] Common suggestions are (1) avoiding overprescription of medications; (2) prescribing less-toxic medications; (3) helping patients understand proper disposal practices for unwanted medications; and (4) providing patients with information about holistic health promotion and illness prevention so patients will require fewer medications. Managing pain with physical therapies can be another effective tool.

Pain Management With Physical Therapies

Physical treatments—including massage and trigger-point therapy, hydrotherapy, traditional physical therapy, pool therapy, therapeutic exercise, osteopathic manipulation, acupuncture, yoga, transcutaneous electrical nerve stimulation (TENS), and prolotherapy—are effective for many types of chronic pain for which individuals commonly take pain medications. A few examples of these therapies are:

Massage therapy. Therapeutic massage is effective for migraine headaches, dysmenorrhea, chronic neck and back pain, muscle spasm, arthritis, and fibromyalgia.[61-65]

Hydrotherapy. Treatment with hydrotherapy is effective for headaches, dysmenorrhea, osteoarthritis, rheumatoid arthritis, chronic low back pain, fibromyalgia, ankylosing spondylitis, and psoriatic arthritis.[66-69]

Physical therapy. Traditional physical therapy is effective for arthritis pain, acute and chronic back dysfunction, neck disorders, headaches, and acute post-traumatic pain.[70-78]

Pool therapy. Many kinds of pain can be effectively treated with pool therapy, including pain associated with spasticity, multiple sclerosis, Parkinson's disease, muscular dystrophy, cerebral palsy, hemiplegia, traumatic brain injury, arthritis, poliomyelitis, peripheral nerve injuries, acute and chronic low-back strain, traumatic injuries, and pain after surgery for muscle and tendon transplants, joint replacements, and bone grafts.[79] Used carefully, physical treatments can alleviate even severe acute pain, such as renal colic and cholelithiasis pain.[80-81]

Physical therapies are effective treatments for pain and do not harm the environment. Until scientists can determine the safety of analgesics in the environment, medical practitioners must deem physical therapies to be a pain-management strategy with fewer environmental pitfalls.

For health-care providers, care of the environment as well as the patient means using physical therapies when possible as the first line of treatment for pain and prescribing medication as a fallback. This will require a change in thinking; prescriptions for powerful analgesics are readily obtainable from most physicians.[82] Instead of prescribing medication for a patient who presents with pain that severe osteoarthritis has caused, a provider could first prescribe physical therapy or recommend regular massage therapy or a water-exercise class; all are known to relieve osteoarthritis pain. If the patient does not get significant pain relief, then medication is a reasonable second option. The American College of Physicians and the American Pain Society give this advice to doctors who treat patients with simple, acute, low-back pain (without spinal stenosis, radiculopathy, or neurological deficits): rather than give patients a prescription for narcotic painkillers, patients should be counseled to stay active, pursue physical therapies, and possibly use a low dosage of an over-the-counter pain reliever.[83]

Conclusion

Analgesics are widely used and a significant part of the problem of pharmaceutical pollution. Physical therapies can be effective for many types of pain, and they cause little or no harm to the environment. Health professionals can contribute to the health of the environment by reducing the load of analgesics they prescribe and encouraging physical therapies as the first line of treatment for patients with pain.

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